

Outing the outliers: Strategy matches oncogene with subtype of prostate cancer

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A new study reveals a previously unidentified candidate oncogene that appears to play a significant role in a subset of prostate cancers. The research, published by Cell Press in the June issue of the journal *Cancer Cell*, describes a new strategy that can be used to find "outlier" genes in cancer subtypes that are not well understood.

"We know that ETS gene fusions occur in 40%-80% of prostate-specific antigen (PSA)-screened prostate cancers, leaving 20%-60% of prostate cancers in which the key genetic aberration is unknown. Further, we have shown that ETS-positive and -negative cancers have distinct transcriptional signatures, suggesting that unique oncogenes and downstream targets play a role in fusion-negative cancers," explains lead author, Dr. Arul M. Chinnaiyan from the University of Michigan Medical School.

Dr. Chinnaiyan and colleagues sought out oncogenes that drive ETS-negative prostate cancers using a refined version of a newly developed approach called, Cancer Outlier Profile Analysis (COPA), that identifies outlier oncogenes in a specific subset of cancer cases. Using this methodology to examine data from seven prostate cancer profiling studies, they identified SPINK1 (serine peptidase inhibitor, Kazal type 1) as being overexpressed in prostate cancer when compared to benign prostate cells and displaying mutually exclusive overexpression with ETS family members.

SPINK1 outlier expression could be detected noninvasively in urine and

SPINK1 outlier expression was shown to be an effective independent predictor of prostate cancer recurrence after surgical resection. Further, the aggressive ETS-negative 22RV1 cell line was identified as a SPINK1 outlier expression model. Reduction of SPINK1 in these cells could reduce invasion, suggesting a functional role for SPINK1 in ETS-negative prostate cancers.

These results identify SPINK1 as a biomarker specific to a subset of aggressive ETS-negative prostate cancers. Further studies are needed to determine the mechanism by which SPINK1 is overexpressed in ETS-negative cancers. "Our study also extends the utility of our original COPA approach by using a meta-COPA strategy to nominate candidate oncogenes in specific types of cancer," concludes Dr. Chinnaiyan.

Source: Cell Press

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